

Current Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Previously Presented) An isolated infectious chimeric parainfluenza virus (PIV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a partial or complete human parainfluenza virus 3 JS (HPIV3 JS) vector genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of HN and/or F glycoproteins of HPIV 1 and/or HPIV2 to form a chimeric PIV genome or antigenome.

2. (Original) The chimeric PIV of claim 1, wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are added adjacent to or within a noncoding region of the partial or complete HPIV3 JS vector genome or antigenome.

3. (Original) The chimeric PIV of claim 1, wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are substituted for one or more counterpart gene(s) or genome segment(s) in a partial HPIV3 JS vector genome or antigenome.

4. (Original) The chimeric PIV of claim 1, wherein said one or more antigenic determinant(s) is/are selected from HPIV1 HN and F glycoproteins and antigenic domains, fragments and epitopes thereof.

5. (Original) The chimeric PIV of claim 4, wherein one or more HPIV1 gene(s) or genome segment(s) encoding one or more HN and/or F glycoprotein(s) or antigenic domain(s), fragment(s) or epitope(s) thereof is/are substituted within the partial or complete HPIV3 JS vector genome or antigenome.

6. (Original) The chimeric PIV of claim 5, wherein both HPIV1 genes encoding HN and F glycoproteins are substituted for counterpart HPIV3 JS HN and F genes in a partial HPIV3 JS vector genome or antigenome.

7. Canceled.

8. (Original) The chimeric PIV of claim 1, wherein one or more HPIV2 gene(s) or genome segment(s) encoding one or more HN and/or F glycoprotein(s) or antigenic domain(s), fragment(s) or epitope(s) thereof is/are added to or incorporated within the partial or complete HPIV3 JS vector genome or antigenome.

9. (Original) The chimeric PIV of claim 6, wherein a plurality of heterologous genes or genome segments encoding different antigenic determinants of HPIV1 and/or HPIV2 are added to or incorporated within the partial or complete HPIV3 JS vector genome or antigenome.

10. (Original) The chimeric PIV of claim 9, wherein said plurality of heterologous genes or genome segments encode antigenic determinants from both HPIV1 and HPIV2 and are added to or substituted within a partial or complete HPIV3 JS vector genome or antigenome.

11. (Original) The chimeric PIV of claim 10, wherein one or more HPIV1 gene(s) or genome segment(s) encoding one or more HN and/or F glycoprotein(s) or antigenic domain(s), fragment(s) or epitope(s) thereof and one or more HPIV2 gene(s) or genome segment(s) encoding one or more HN and/or F glycoprotein(s) or antigenic domain(s), fragment(s) or epitope(s) thereof is/are added to or incorporated within the partial or complete HPIV3 JS vector genome or antigenome.

12. (Original) The chimeric PIV of claim 11, wherein both HPIV1 genes encoding HN and F glycoproteins are substituted for counterpart HPIV3 JS HN and F genes to form a chimeric JS HPIV3-1 vector genome or antigenome which is further modified by addition or incorporation of one or more gene(s) or gene segment(s) encoding one or more antigenic determinant(s) of HPIV2.

13. (Original) The chimeric PIV of claim 12, wherein a transcription unit comprising an open reading frame (ORF) of an HPIV2 HN gene is added to or incorporated within the chimeric JS HPIV3-1 vector genome or antigenome.

14. (Original) The chimeric PIV of claim 13 selected from JS rPIV3-1.2HN, or JS rPIV3-1_{cp45}.2HN.

15. (Original) The chimeric PIV of claim 1, wherein the chimeric PIV genome or antigenome is attenuated by addition or incorporation of one gene or cis-acting regulatory element from a bovine PIV3 (BPIV3).

16. (Original) The chimeric PIV of claim 1, wherein the chimeric PIV genome or antigenome incorporates one or more heterologous, non-coding non-sense polynucleotide sequence(s).

17. (Original) The chimeric PIV of claim 1, wherein the chimeric genome or antigenome encodes a chimeric glycoprotein having antigenic domains, fragments, or epitopes from both HPIV3 JS and HPIV1 or HPIV2.

18. (Original) The chimeric PIV of claim 17, wherein the heterologous genome segment encodes a heterologous glycoprotein ectodomain which is substituted for a corresponding glycoprotein ectodomain in the vector genome or antigenome.

19. (Original) The chimeric PIV of claim 1, wherein the chimeric genome or antigenome is modified by introduction of an attenuating mutation involving an amino acid substitution of phenylalanine at position 456 of the HPIV3 L protein.

20. (Original) The chimeric PIV of claim 19, wherein phenylalanine at position 456 of the HPIV3 L protein is substituted by leucine.

21. (Previously Presented) The chimeric PIV of claim 1, wherein the chimeric genome or antigenome incorporates at least one and up to a full complement of attenuating mutations present within HPIV3 JS *cp45*.

22. (Previously Presented) The chimeric PIV of claim 1, wherein the chimeric genome or antigenome incorporates at least one and up to a full complement of attenuating mutations specifying an amino acid substitution in the L protein at a position corresponding to

Tyr₉₄₂, Leu₉₉₂, or Thr₁₅₅₈ of in JS *cp45*; in the N protein at a position corresponding to residues Val₉₆ or Ser₃₈₉ of JS *cp45*, in the C protein at a position corresponding to Ile₉₆ of JS *cp45*, in the F protein at a position corresponding to residues Ile₄₂₀ or Ala₄₅₀ of JS *cp45*, in the HN protein at a position corresponding to residue Val₃₈₄ of JS *cp45*, a nucleotide substitution in a 3' leader sequence of the chimeric virus at a position corresponding to nucleotide 23, 24, 28, or 45 of JS *cp45*, and/or a mutation in an N gene start sequence at a position corresponding to nucleotide 62 of JS *cp45*.

23. (Original) The chimeric PIV of claim 21, wherein the chimeric genome or antigenome includes at least one attenuating mutation stabilized by multiple nucleotide changes in a codon specifying the mutation.

24. (Original) The chimeric PIV of claim 1, wherein the chimeric genome or antigenome incorporates one or more heterologous gene(s) or genome segment(s) encoding one or more respiratory syncytial virus (RSV) F and/or G glycoprotein(s) or immunogenic domain(s), fragment(s), or epitope(s) thereof.

25. (Previously Presented) The chimeric PIV of claim 1 which is a complete virus.

26. (Original) The chimeric PIV of claim 1 which is a subviral particle.

27. (Withdrawn) A method for stimulating the immune system of an individual to induce protection against parainfluenza virus (PIV) which comprises administering to the individual an immunologically sufficient amount of the chimeric PIV of claim 1 combined with a physiologically acceptable carrier.

28. (Withdrawn) The method of claim 27, wherein the chimeric PIV is administered in a dose of 10^3 to 10^7 PFU.

29. (Withdrawn) The method of claim 27, wherein the chimeric PIV is administered to the upper respiratory tract.

30. (Withdrawn) The method of claim 27, wherein the chimeric PIV is administered by spray, droplet or aerosol.

31. (Withdrawn) The method of claim 27, wherein the chimeric PIV elicits an immune response against one or both of HPIV1 and HPIV2.

32. (Withdrawn) The method of claim 27, wherein the chimeric PIV elicits a polyspecific immune response against multiple HPIVs.

33. (Withdrawn) The method of claim 27, wherein the chimeric PIV and a second recombinant PIV are administered sequentially or simultaneously to elicit a polyspecific immune response.

34. (Original) An immunogenic composition to elicit an immune response against parainfluenza virus (PIV) comprising an immunogenically sufficient amount of the chimeric PIV of claim 1 in a physiologically acceptable carrier.

35. (Original) The immunogenic composition of claim 34, formulated in a dose of 10^3 to 10^7 PFU.

36. (Original) The immunogenic composition of claim 34, formulated for administration to the upper respiratory tract by spray, droplet or aerosol.

37. (Original) The immunogenic composition of claim 34, wherein the chimeric PIV elicits an immune response against one or more virus(es) selected from HPIV1, HPIV2 and HPIV3 JS.

38. (Original) The immunogenic composition of claim 34, wherein the chimeric PIV elicits an immune response against HPIV3 JS and another virus selected from HPIV1 and HPIV2.

39. (Previously Presented) An isolated polynucleotide comprising a chimeric parainfluenza virus (PIV) genome or antigenome which includes a partial or complete human

parainfluenza virus 3 JS (HPIV3 JS) vector genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of HN and/or F glycoproteins of one or both of HPIV1 and HPIV2 to form a chimeric PIV genome or antigenome.

40. (Original) The isolated polynucleotide of claim 39, wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are added adjacent to or within a noncoding region of the partial or complete HPIV3 JS vector genome or antigenome.

41. (Original) The isolated polynucleotide of claim 39, wherein said one or more heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are substituted for one or more counterpart gene(s) or genome segment(s) in a partial PIV vector genome or antigenome.

42. (Original) The isolated polynucleotide of claim 39, wherein the chimeric genome or antigenome is attenuated by incorporation of one gene or cis-acting regulatory element from a bovine PIV3 (BPIV3).

43. (Original) The isolated polynucleotide of claim 39, wherein the chimeric genome or antigenome encodes a chimeric glycoprotein having antigenic domains, fragments, or epitopes from two or more different HPIVs.

44. (Original) The isolated polynucleotide of claim 39, wherein the chimeric genome or antigenome is further modified by incorporation of an attenuating mutation involving an amino acid substitution of phenylalanine at position 456 of the HPIV3 L protein.

45. (Original) The isolated polynucleotide of claim 39, wherein phenylalanine at position 456 of the HPIV3 L protein is substituted by leucine.

46. Canceled

47. (Previously Presented) The isolated polynucleotide of claim 39, wherein the chimeric genome or antigenome incorporates one or more heterologous gene(s) or genome segment(s) encoding one or more respiratory syncytial virus (RSV) F and G glycoprotein(s) or immunogenic domain(s), fragment(s), or epitope(s) thereof.

48. (Withdrawn/Previously Presented) A method for producing an infectious attenuated chimeric parainfluenza virus (PIV) particle from one or more isolated polynucleotide molecules encoding said PIV, comprising:

expressing in a cell or cell-free lysate an expression vector comprising an isolated polynucleotide comprising a partial or complete human parainfluenza virus 3 JS (HPIV3 JS) vector genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of HN and/or F glycoproteins of HPIV1 and/or HPIV2 to form a chimeric PIV genome or antigenome, and PIV N, P, and L proteins.

49. (Withdrawn) The method of claim 48, wherein the chimeric PIV genome or antigenome and the N, P, and L proteins are expressed by two or more different expression vectors.

50. (Withdrawn/Previously Presented) An expression vector comprising an operably linked transcriptional promoter, a polynucleotide sequence which includes a partial or complete human parainfluenza virus 3 JS (HPIV3 JS) vector genome or antigenome combined with one or more heterologous gene(s) or genome segment(s) encoding one or more antigenic determinant(s) of HN and/or F glycoproteins of HPIV1 and/or HPIV2 to form a chimeric PIV genome or antigenome, and a transcriptional terminator.

51. (Original) The chimeric PIV of claim 6, wherein the chimeric genome or antigenome incorporates at least one and up to a full complement of attenuating mutations present within HPIV3 JS cp45 selected from mutations specifying an amino acid substitution in the L protein at a position corresponding to Tyr942, Leu992, or Thr1558 of JS cp45; in the N protein at a position corresponding to residues Va196 or Ser389 of JS cp45, in the C protein at a

Appl No. 09/458,813
Amdt. dated June 8, 2004
Reply to Office Action of Oct. 2, 2003

position corresponding to Ile96 of JS cp45, a nucleotide substitution in a 3' leader sequence of the chimeric virus at a position corresponding to nucleotide 23, 24, 28, or 45 of JS cp45, and/or a mutation in an N gene start sequence at a position corresponding to nucleotide 62 of JS cp45.

52. (Original) The isolated polynucleotide of claim 39, wherein the chimeric genome or antigenome incorporates at least one and up to a full complement of attenuating mutations present within HPIV3 JS cp45.